REMARKS

Entry of the above amendments and reconsideration of this application are requested. Upon entry of the amendments, this application will contain claims 20-28, 43-45, and 49-84. Of these, claims 20-28 and newly added claims 49-62 are drawn to the elected invention (cardiomyocyte cell), and claims 43-45 and newly added claims 63-84 are drawn to methods of using a cardiomyocyte cell (potential rejoinder claims, presently withdrawn from consideration). Newly added claims 49-84 are fully supported by the specification and introduce no new subject matter. Support for these claims may be found, for example, in the discussions of nucleotide sequences, amino acid sequences, and functional properties found at pages 10-14 of the application, in the discussions of screening methods spanning pages 22-23 of the application, and in the original claim set. As well, it is believed that no new fees are required for entry of the new claims, as they are of a number and type such that their associated fees are encompassed by the fees of the cancelled claims (Canceled: 36 total, 7 independent; Added: 36 total, 2 independent). Entry of these new claims is therefore requested.

Turning now to the points raised in the Office Action, claim 20 was objected to for informalities. In particular, the Action stated that an article needed to be inserted between "having" and "introduced". In response, claim 20 has been amended in this fashion. It is believed that the current or former usage would be proper and fully understood by the skilled artisan.

Claims 20-28 stand rejected under 35 U.S.C., first paragraph, "because the specification, while being enabling for a cardiomyocyte having an introduced nucleic

acid encoding a cyclin D2 protein comprising SEQ. ID NO: 2, SEQ. ID NO: 4 or the sequence of a mouse cyclin D1 protein as described by Soonpa *et al.* (1997) *J. Clin. Invest.* 99:2644-2654 in the paragraph bridging the left and right column on page 2645, does not reasonably provide enablement for a cardiomyocyte cell having introduced a nucleic acid encoding any protein having cyclin D2 activity." This rejection is respectfully traversed.

As stated in MPEP §2164, "the purpose of the enablement requirement is to ensure that the invention is communicated to the interested public in a meaningful way." The standard is whether the specification teaches a person of ordinary skill in the art to make and/or use the claimed invention without undue experimentation. As this standard provides, a significant degree of experimentation is permissible under the standards of enablement, especially where the experimentation would involve routine procedures.

In the present set of facts, **(1)** as acknowledged by the Examiner in the Office Action, the degree of ordinary skill in the relevant field is high; **(2)** the sequences involved are known, and were known for some time prior to the filing date of this application (see, e.g. U.S. Patent No. 5,869,640 cited at page 8 of the application and incorporated by reference); **(3)** the relevant art had developed with regard to functional domains of the sequences involved as of the filing date of this application (including, for example, functional studies of domains that overlap in cyclins D1, D2, and D3); **(4)** the specification identifies for skilled artisan not only **(i)** a variety of substitutions (see e.g., page 11, line 14 to page 12, line 13) but also **(ii)** domains that differ among cyclin D2 and cyclins D1 and D3 to assist the skilled artisan in making polypeptides that retain the characteristic cyclin D2 activity (see, e.g., Table

1 and the discussions at page 10, lines 13 to 21 and page 12, line 30 to page 13, line 20), and **(iii)** distinct, characterizing functions of cyclin D2 (see, e.g. page 13, lines 16-20, Table 2 and discussions thereof at page 10, and Examples).

In making this enablement determination, it is important to understand that a person of ordinary skill in the art, when setting out to practice the invention, would not as a first step attempt to compile a list of all possible differing sequences that could possibly satisfy structural and functional features, and then test all sequences in the list for functionality. Rather, one would be expected to begin with a reference sequence set forth in the specification, assess what changes could be made with an expectation of success and perform routine procedures to determine whether the sequence has the characteristics described and claimed in the application. In this manner, the specification enables of person of ordinary skill in the art to easily identify variants that are within the scope of the invention. This could certainly be done without undue experimentation in view of the specification and the high level of skill in the art at the time the application was filed. Indeed, very little experimentation would be required for a person of ordinary skill in the art to identify a number of changes that could be made to a disclosed reference sequence that would not be expected to eliminate the functionality of the encoded protein, and then to test the resulting polynucleotide or protein to confirm activity.

Still further, at the time the application was filed, a variety of computer programs were commercially available that predict the 3-dimensional structure of polypeptides, and that predict how changes to the polypeptide sequence will affect the 3-D structure. An example of such a program is the program DSSP (Kabsh, W. & Sander, S. (1983) Secondary structure definition by the program DSSP.

Biopolymers 22:2577-2637), which can be used to predict secondary structure of protein folding. Further, higher folding levels of a protein can be predicted using the programs PROCHECK, Raster3D and MOLSCRIPT (Laskowski, R.A., MacArthur, M.W. Moss, D.S. & Thornton, *J.M.* (1993). PROCHECK-a program to check the stereochemical quality of protein structures. *J. Appl.Cryst.* 26:283-291; Bacon, D.J. & Anderson, W.F. (1988). A fast algorithm for rendering space-filling molecule pictures. *J. Mol. Graph.* 6:219-220; Merrit, E.A. & Murphy, M.E.P. (1994). Raster3D version 2.0 - a program for photorealistic molecular graphics. *Acta Cryst.* D 50:869-873; and Kraulis, P.J. (1991). MOLSCRIPT: a program to produce both detailed and schematic plots of protein structures. *J. Appl. Cryst.* 24:946-950). Applicant submits that the availability of such modeling software would also assist a person of ordinary skill in the art in predicting the effects of amino acid changes in carrying out the claimed invention.

For at least these reasons, the Applicant submits that the enablement requirement of 35 U.S.C. §112, first paragraph is satisfied for claims 20-28, and respectfully requests that the subject rejection be withdrawn.

Claim 21 stands rejected under 35 U.S.C. §112, second paragraph, based upon an assertion that it is indefinite because of its use of "corresponding to" and "substantial identity to". In response, claim 21 has been amended to change the phrase "corresponding to" to "of" to moot the related issue. As to "substantial identity to", it is submitted that this terminology is definite. In making this assessment, claim terminology is to be read in light of the specification. At page 11, lines 14-17, this term is defined for the skilled artisan -- "substantial identity" encompasses proteins that differ from the native D2 sequences but which are

sufficiently identical to exhibit the characteristic cyclin D2 activity as identified in the application (see specific discussions thereof provided above). As such, those of ordinary skill will understand the metes and bounds of this terminology, and withdrawal of the subject rejection is therefore solicited.

Claims 20, 21, 23, 24, 26 and 27 stand rejected under 35 U.S.C. § 102(b) "as being anticipated by Soonpa *et al.* (1997) *J. Clin. Invest.* 99:2644-2654 as evidenced by Lahti *et al.* (1997) *J. Biol. Chem.* 272: 10859-10869." This rejection is respectfully traversed.

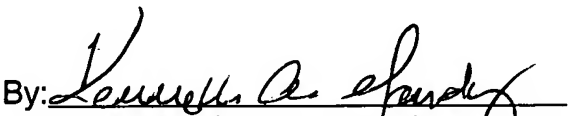
In making this rejection, the Office Action proposes a construction of the language "a cyclin D2 protein" to encompass a native cyclin D1 protein disclosed in the work of Soonpa *et al.* (1997). This is evident from both the specific passages of this rejection given at pages 9-10 and the "Claim construction" commentary given at pages 2-3 of the Office Action. It is submitted, however, that such a construction is innappropriate. To make this construction, one has to conclude that a person of ordinary skill in the art, reading the claims in light of the specification, would understand that the Applicant intended that "a cyclin D2 protein" would encompass a native cyclin D1 protein. It is inconceivable that such a conclusion could be reached from the present application. The application goes out of its way to distinguish the characteristics of cyclin D2 proteins from those of cyclin D1 proteins in the context of the invention, for example in Table 2 and the discussions that follow on page 10 of the application. Accordingly, it is submitted that this rejection is unsupported, and its withdrawal is respectfully solicited.

As noted above, new claims 49-84 have been added to the application. Of these, claims 49-62 are drawn to the elected invention (cardiomyocyte cells), and

favorable consideration and allowance of these claims are requested. In addition, new claims 63-84 are drawn to methods of using cardiomyocyte cells (potential rejoinder claims). Favorable consideration, rejoinder and allowance of these claims are requested upon the basis of the allowance of the elected claims.

In view of the foregoing, reconsideration and allowance of this application containing claims 20-28, 43-45, and 49-84 are respectfully requested. The Examiner is invited to contact the undersigned attorney by telephone if there are any questions about this submission or other matters that may be readily handled by phone to expedite the allowance of this application.

Respectfully Submitted,

By: 

Kenneth A. Gandy, Reg. No. 33,386
Woodard, Emhardt, Moriarty,
McNett & Henry LLC
Bank One Center/Tower
111 Monument Circle, Suite 3700
Indianapolis, Indiana 46204-5137
(317) 634-3456